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EXAMINER	
STANDLEY, STEVEN H	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,517	SCHENK ET AL.	
	Examiner	Art Unit	
	Steven Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46,48,50-76 and 78-80* is/are pending in the application.

4a) Of the above claim(s) *1-40 and 56-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-46,48,50-55,71-76 and 78-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SDD

RESPONSE TO AMENDMENT

1. This action is supplemental to the office action of 29 September 2005 and replaces that action in its entirety, except that cited art is provided in that office action, as is the form 892.

The amendment filed 7/01/05 has been made of record. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action. Claims 1-46, 48, 50-76, and 78-80 are pending in this application. Claims 41-46, 48, 50-55, 71-76, and 78-80 are under consideration. Claims 1-40 and 56-70 are withdrawn from consideration as being drawn to a non-elected invention.

Objections/Rejections: Withdrawn

Claim Objections

2. The objection to claim 43 as a dependent claim that fails to limit is withdrawn due to applicant's amendment.

Claim Rejections - 35 USC § 112

3. The rejection of claims 41-43, 45-48, 50-55, 71-73, and 75-80 under 35 USC § 112, 1st paragraph, as lacking enablement for agents other than immunogenic Aβ is withdrawn in response to applicant's amendment.

4. The rejection of claims 44 and 74 under 35 USC 112, 1st paragraph, as lacking enablement for other agents is withdrawn in response to applicant's amendment.

5. The rejection of claims 41 and 71 under 35 USC 112, 1st paragraph, as lacking written description of immunogenic agents is withdrawn in response to applicant's amendment.

6. The rejection of claims 43 and 73 under 35 U.S.C. 112, 1st paragraph, as lacking written description of Aβ epitopes is withdrawn in response to applicant's arguments.

7. The rejection of claims 44 and 74 under 35 U.S.C. 112, 1st paragraph, as lacking written description of immunogenic agents is withdrawn in response to applicant's amendment.

8. The rejection of claims 43 and 73 under 35 U.S.C. 112, 2nd paragraph, as indefinite in the recitation of "fragment" is withdrawn in response to applicant's amendment.

Objections/Rejections: Maintained/New Grounds

Claim Objections

9. Claim 78 is objected to because of the following informalities: Claim 78 depends from a cancelled claim. Appropriate correction is required.

Double Patenting

10. The rejection of claims 41, 42, 45, 47, 48, 71, 72, 75, 77, and 78 under the judicially-created doctrine of obvious double-patenting as unpatentable over the '138, '139, '140, '143, '144, '849, '850, '427, and '888 patents is maintained for the reasons made of record in the office action dated 4/07/05 and newly applied to claims 46 and 76.

Applicant has amended claims 41, 44 and 74 to recite a Markush group of "Lewy body diseases." Applicant argues that neither the patents nor the secondary reference, Kotzbauer et al, teach that the therapeutic strategies directed to inhibition or reduction of Aβ deposits are likely to be successful in LBD distinct from AD.

Applicant's amendment and arguments have been fully considered but have not been found to be sufficient to overcome the rejections. It is agreed that Kotzbauer does not address the role of Aβ deposits in LBD. However, the nexus between the pathology of LBD and of AD was well known in the art at the time the instant application was filed. In their analysis of the clinical

pathology of LBD, Hansen et al. (Chapter 14 of Functional Neurobiology of Aging, 2001) indicate that "most, but not all, dementia with lewy bodies [for instance] have more AD pathology than age-matched controls [page 176, right column, top]." The patients would also present with dementia indistinguishable from that of AD, and therefore would be treated the same and be part of the same patient population. Hansen et al. go on to state, "If neocortical amyloid is on hallmark for neuropathologic diagnosis of AD, then most LDB brains have concomitant AD. Most LBD brains not only have as much neocortical amyloid as AD specimens when measured immunocytochemically, but typically have as many neuritic plaques as AD brains and far more than age-matched controls. Therefore, they meet the 1985 NIA criteria for AD and because many of the plaques are neuritic, albeit usually lacking tau-positive neuritis, they also typically qualify as 'definite or 'probable' AD according to criteria from the consortium to establish a registry for AD."

Therefore, patients present both cognitively and pathologically as AD patients and would be treated as such, and the instant claims are not patentably distinct from those of the cited patents.

Claims 46 and 76 are newly included in this rejection because they differ from the rejected claims only in that they recite dosage regimens. MPEP §2144.05 states that optimization of ranges such as are specified in these claims is routine experimentation that does not render an invention unobvious.

Applicant speculates that claims drawn to other specific Lewy Body diseases were omitted from this rejection because it was recognized that there was no indication that Lewy

Body Diseases other than Alzheimer's disease could be treated as claimed. These claims were in fact omitted because the cited patents do not address these species of disease..

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 41-46, 48, and 50-55 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating patients suffering from Alzheimer's or Parkinson's disease by administering immunogenic Aβ, does not reasonably provide enablement for "therapeutically treating" any disease, nor does it provide enablement for treatment of any disease other than Parkinson's disease and Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 71-76 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 71-76 and 78-80 are drawn to prophylaxis. Claims 41-46, 48, and 50-55 are drawn to "therapeutic" treatment.

Stedman's medical dictionary (27th edition) defines "prophylaxis" as

Prevention of disease or of a process that can lead to disease.

"Therapeutic" is defined as

> Relating to therapeutics or to the treatment, remediating, or curing of a disorder or disease. [G. *therapeutikos*1]

Thus the claims encompass both preventing and curing Lewy Body diseases. Neither the prior art nor the instant specification provides guidance to indicate that any of these diseases can be either prevented or cured. Vickers (Drugs Aging 2002, vol. 19(7) pp. 487-494) teaches that there is "no effective treatment currently available to reverse, slow down, or prevent" Alzhiemer's disease and most brain diseases (p. 487, column 1).

Claims 44-46, 48, 53-55, 71-76, and 78-80 encompass treatment of numerous diseases. The nature of this invention is thus highly complex, and is a method for treating a Lewy body disease that encompasses 18 different designations of the disease (see Hansen et al.). Therefore the invention attempts to treat generically a variety of diseases with different characterizations, different etiologies, cell populations affected, and highly variable neuropathological alterations and severities.

The prior art teaches 18 different characterizations of "a Lewy body disease [see Hansen et al., table 14.1]." It also teaches that the diseases have different characterizations, and the genetic etiologies characterized thus far indicate many proteins are linked to Parkinson's. For instance, at the time the invention was filed there were already at least 5 known gene linkages, suggesting the origins of a Lewy body disease are variable (see table 14.3, Hansen et al.). Moreover, because the art teaches that most LBDs are associated with Aβ deposition and therefore meet the criterion for 'definite' or 'probable' AD (as described above under the Obviousness Double Patenting) rejection, one skilled in the art would not know what other distinct diseases the invention would be useful for. Furthermore, as it relates to the use of antibodies, or passive immunization, the inventor's own post filing dated work indicates that it is not known if antibody treatment of PD mice results in improvement of behavioral or cognitive deficits (Masliah et al.., Neuron, 2005, vol. 46, pp. 857-868,)

The specification provides a few examples of a mouse models of AD and PD, and AD/PD crossed mice and their treatment with Aβ. The treatments reduce Aβ or synuclein plaques or deposits. However the specification does not teach how to treat any other Lewy Body disease, nor are the mice used representative of generic "lewy body diseases." They are, in fact, understood to be mouse models of AD and PD, and to the extent that AD and PD are not part or whole of any given LBD, the models and treatments are insufficient in disclosing treatment of the non-AD diseases characterized by Lewy bodies. The specification does not teach the use of passive immunization as a bona fide treatment of PD or any other disease. The inventor's own post-filing date disclosure indicates that, even now (2005), "...further development of this approach might have a potential place in treatment of LBD [Masliah et al. page 865, left

column]," indicating it is really unknown, even at the present time, whether the applicant's invention will work at all in the treatment of LBD. Therefore, it is also unpredictable as to whether the applicant's invention will work.

Therefore, given the complex nature of the invention, the contradictory nature of the prior art, the lack of working examples and guidance from the specification, and the unpredictability of the art, it would require undue experimentation for one skilled in the art to make or use the invention as currently claimed.

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. The rejection of claims 41, 42, 44, 45, 50, 54, 55, 71, 74, and 75 under 35 USC § 102(e) as anticipated by US2002/0187157 and US2003/000086938 is maintained for the reasons made of record in the office action dated 4/07/05 and newly applied to claims 46, 48, 51-53, 72, 76, and 78-80. Each reference teaches the limitations of each of the cited claims.

Applicant argues that the Jensen applications do not intend to treat diseases such as Parkinson's.

Applicant's arguments have been fully considered and not found to be persuasive. The applicant is directed to the section of each of the Jensen et al. publications, called "Background of the Invention," wherein it is stated that "amyloid is associated with diseases such as systemic amyloidosis, AD, maturity-onset diabetes, ***Parkinson's disease***, etc." Applicant is next directed

to claim 34 of Jensen et al. 2002 and claim 27 of Jensen et al. 2003 wherein "a method for treating...Alzheimer's...or other diseases and conditions characterized by amyloid deposits..." The methods relates to the administration of Aβ (see claim 20 of the 2002 publication and claim 27 of the 2003 publication). Since "amyloid is associated with...Parkinson's" and Jensen et al. claim treating "diseases and conditions characterized by amyloid deposits," Jensen intends to treat Parkinson's disease. Claims 46, 48, 51-53, 72, 76, and 78-80 were omitted from the original rejection. However, the multiple doses of claims 46 and 76 are taught in paragraph 157 of each of the publications. Patients suffering from a disease clearly have a risk factor for that disease; thus claims 48 and 78 are anticipated. The improvements of claims 51 and 52 are inherent in a successful outcome. Monitoring, as claimed in claim 53, is inherent in the methodology described in paragraphs 178 and 179 of each publication. Claim 72 limits the agent administered to what is clearly taught in the publications, administration of Aβ or a fragment. Patients suffering from Parkinson's do not inherently also suffer from Alzheimer's or have risk factors for it; thus claims 79 and 80 are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 41, 43-46, 48, 50-55, 71, 73-76, and 78-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Jensen et al. publications.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The Jensen et al. publications teach as set forth above but fail to teach administration of an antibody. However, it would be obvious to one of ordinary skill in the art to administer antibodies instead of immunogenic peptides One of ordinary skill in the art would be motivated to do so because induction of antibodies is the goal of vaccination with peptides, and thus the artisan would expect similar success from administering an antibody.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Janet L. Andres, Ph.D.
30 September 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER